



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/517,328	12/09/2004	Jeffrey A Smith	00789-05	7405
34444	7590	09/05/2006	EXAMINER	
UNIVERSITY OF VIRGINIA PATENT FOUNDATION 250 WEST MAIN STREET, SUITE 300 CHARLOTTESVILLE, VA 22902			KRISHNAN, GANAPATHY	
			ART UNIT	PAPER NUMBER
			1623	

DATE MAILED: 09/05/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.		Applicant(s)	
	10/517,328		SMITH ET AL.	
	Examiner		Art Unit	
	Ganapathy Krishnan		1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 23 June 2006.
- 2a) ☒ This action is FINAL. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-9, 21-38 and 48-50 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-9, 21-38 and 48-50 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date: _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date: _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

The amendment filed 6/23/2006 has been received, entered and carefully considered.

The following information provided in the amendment affects the instant application:

1. New Claims 48-50 have been added.
2. Claim 29 has been amended.
3. Claims 10-20 and 39-47 have been withdrawn.
4. Remarks drawn to objections to the abstract, claims and rejections under 35 USC 112, first and second paragraphs, 102 and 103.

Claims 1-9, 21-38 and 48-50 are under examination.

Specification

The first page of the WIPO document filed 12/9/2004, which has an abstract, has also been used as the abstract sheet in the instant specification. This is not acceptable if the instant claims are determined to be allowable at a later stage. The Office requires the abstract to be typed on a separate sheet of paper even though applicants intend using the abstract on the WIPO document for the instant application. Hence, applicants are requested to kindly type the abstract appearing on the first page of the WIPO document (WO 03/105766) on a separate sheet and file the same.

Priority

The priority claim recited in the Preliminary Amendment of 12/9/2004 is acknowledged.

Claim Objections

The objection to claim 29 has been overcome by amendment.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 21-24 and 48-50 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of some particular and specific neoplastic tumors or cancers, does not reasonably provide enablement for the treatment of any other disease or conditions characterized by inappropriate activity is being maintained for reasons of record.

Applicants have traversed the rejection by arguing that:

1. Inappropriate Rsk activity refers to over expression of Rsk, excessive kinase activity of Rsk or that there is expression of Rsk activity where there is normally no such activity.
2. At the time of filing of this application several disease states were suggested to involve inappropriate Rsk activity and cite references and diseases and that inhibition of Rsk is sufficient to reverse a disease state. The data in the specification, examples 4 and 5 demonstrate various kinds of cancer cell lines. The specification gives concentrations of the active agents that inhibit Rsk activity and one of ordinary skill in the art would be able to apply it to any disease with inappropriate activity.
3. One of ordinary skill in the art would be able to routinely screen compounds for the desired activity (inhibiting Rsk) and having to do so is not undue.

Art Unit: 1623

Applicants' arguments are not found to be persuasive.

Firstly, it is respectfully pointed out that applicants' have to list the cited eleven non-patent literature references at page 17 of their response in support of their statement regarding the disease states that have been suggested to involve inappropriate Rsk activity in an Information Disclosure Statement.

The term inappropriate Rsk activity as recited in the claims is not seen to be limited only to those applicants state above. It is also seen to include any activity other than the ones recited by applicants in the specification including ones that are not known yet. One of ordinary skill in the art will not understand the claim recitation as limiting to only the activities applicants refer.

Regarding the disease states that are suggested to involve inappropriate Rsk activity, applicants cite references that suggest several diseases whose etiology is not seen to be attributed to Rsk activity alone. The diseases listed are known to involve other factors not just Rsk activity. Hence, one of ordinary skill in the art will not expect to treat all of these diseases including ones not yet know just by inhibiting Rsk activity. The examples in the instant specification uses specific flavones to demonstrate inhibition of Rsk. The instant claims recite administration of a composition comprising an Rsk specific inhibitor. One of ordinary skill in the art will not extrapolate the activity of the flavones provided in the instant specification to any other compound or composition. In this respect undue experimentation is required to determine if a given compound or composition is an Rsk inhibitor before it can be considered for use in the said method. The specification also gives examples that use breast cancer and prostate cancer cell lines. One of ordinary skill in the art will not extrapolate the results seen with these cell lines to the treatment of all other forms of cancer as instantly claimed in claim 49 and encompassed by

Art Unit: 1623

the recitation in claim 48. Enablement is seen only for the specific flavones of formula I-III for the treatment of breast cancer and prostate cancer.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 21-32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is being maintained for reasons of record.

The claim recitation in instant claims 21 and 25 are broad and are not clear as to what applicants intend. The specific activity has to be recited in the claims. Limitations from the specification cannot be read into the claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 4-9 are rejected under 35 U.S.C. 102(b) as being anticipated by Matthes et al (Phytochemistry, 1980, 19, 2643-2650).

Applicants argue that the present claims are drawn to a pharmaceutical composition and Matthes does not disclose a pharmaceutical composition and hence does not anticipate the instant claims.

Art Unit: 1623

Matthes et al disclose a compound of structural formula 7, wherein two of the three hydroxyl groups on the sugar moiety are acetylated (page 2645). This compound is structurally same as the compound claimed in instant claims 1 and 4-9. Matthes discloses an ethanol solution of the compounds of his invention. The ethanol solution of the compound of formula 7 of Matthes is a pharmaceutical composition (limitation of claim 1) since ethanol is a known pharmaceutically acceptable carrier. Matthes may not have recited the term pharmaceutical in his disclosure. Still the disclosure of Matthes reads on the instant claims.

Claims 25-27 are rejected under 35 U.S.C. 102(b) as being anticipated by Bjorbaek et al (WO 00/66721) is being maintained for reasons of record.

Applicants argue that Bjorbaek does not teach or even contemplate “inappropriate Rsk activity” and that Bjorbaek has no evidence that inhibition of Rsk activity will alter the rate of weight gain and it cannot be deduced from his disclosure inhibition of Rsk activity alone would alter rate of weight gain. This is not found to be persuasive.

Bjoebaek et al teach a method of modulating body weight, fat content, leptin levels or oxygen consumption by altering or modulating Rsk activity using nucleic acid construct expressing Rsk2 or a biologically active fragment thereof (page 2, lines 1-13; page 21, lines 1-7; example at pages 24 through 31;) This teaching reads on treatment of disease/condition characterized by inappropriate Rsk activity as instantly claimed. The instant claims are not drawn to altering rate of weight gain.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 2-3 and 33-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Matthes et al (Phytochemistry, 1980, 19, 2643-2650) in combination with Bjorbaek et al (WO 00/66721), Marks et al (US 5,910,583) and Kuijpers et al (US 5,733,523) is being maintained for reasons of record.

Applicants argue that:

1. The present specification discloses that inhibition of Rsk catalytic activity halts the growth of tumor cells and the reversal of the diseases state. The compound of Matthes , especially compound 7 was slightly cytotoxic and hence teaches away from the use of compound 7 and Matthes does not contemplate compositions or methods useful for treating diseases or condition wherein the composition is an Rsk specific inhibitor.

2. The disclosure of Dai (cited by applicants in the response) and the citation by NCI teach away from the use of compounds of claim 1 because the compound of Mathes is similar to that disclosed in the references and have no antitumor activity.

3. Bjorbaek speculates about regulating Rsk and not inhibiting it. Kuijpers and Mark do not correct the deficiencies of the other references because there is no suggestion of an Rsk inhibitor. Hence there is not motivation to combine the instant prior art.

Applicants' arguments are not found to be persuasive.

Art Unit: 1623

Matthes et al disclose a compound of structural formula 7, wherein two of the three hydroxyl groups on the sugar moiety are acetylated (page 2645). This compound is structurally same as the compound claimed in instant claims 1 and 4-9. Hence, compound 7 of Matthes should be an inhibitor of Rsk and should reverse the diseased state as instantly claimed. The structure of the compound shown in the NCI citation is 4'-O-acetylafzelin, which has only one acetyl group on the sugar moiety. This is not the same as the one disclosed by Matthes.

Compound 7 of Matthes also reads on the structures as instantly claimed and hence is an Rsk inhibitor and could be used for making compositions as instantly claimed. Even though Matthes may not contemplate Rsk activity inhibition the compound disclosed by Matthes is the same as claimed instantly and hence should have the same properties. A compound and its properties are inseparable. He also discloses that compound 7 is slightly cytotoxic to hepatoma cell lines.

Bjoebaek et al teach a method of modulating body weight, fat content, leptin levels or oxygen consumption by altering or modulating Rsk activity using nucleic acid construct expressing Rsk2 or a biologically active fragment thereof (page 2, lines 1-13; page 21, lines 1-7; example at pages 24 through 31). The compounds of their invention can be used in the form of compositions (page 23, line 8 through page 24, line 20).

Kuijpers et al teach in general the use of antisense oligonucleotides and their pharmaceutical formulations for the treatment of tumors (see abstract, col. 1, lines 26-40) and Marks teaches in general a variety of uses for oligonucleotide formulations including treatment of tumors (col. 5, lines 9-25).

Based on the teachings of the prior art above it would have been obvious to one of ordinary skill in the art at the time the invention was made to make a composition comprising an

Art Unit: 1623

Rsk specific inhibitor and an antitumor agent including extracts from Zingiber zerumbet as instantly claimed because pharmaceutical compositions comprising such active agents are individually taught in the prior art to have the same utility.

From the disclosure of the prior art it can be seen that the Rsk activity of the compound of Matthes is inherent since it is structurally the same as the one instantly claimed. Bjobaek teaches the use of modulating the Rsk activity using nucleic acids. Kuijpers and Marks are drawn to treatment of tumors using antisense oligonucleotides and oligonucleotides respectively. Hence it would have been prima facie obvious to one of ordinary skill in the art to combine the teachings given above.

Conclusion

Claims 1-9, 21-38 and 48-50 are rejected

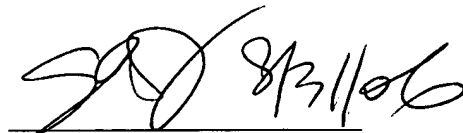
THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

Art Unit: 1623

however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

GK

A handwritten signature in black ink, followed by the date 8/31/06. The signature is stylized and appears to be 'SJ' followed by a flourish.

Shaojia Jiang
Supervisory Patent Examiner
Art Unit 1623